Remarks

Claims 1-8 are currently under examination. Claim 2 has been canceled. Claims 1 and 3 have been amended and new claims 21-48 have been added. Support for the claim amendments and new claims can be found throughout the Specification and the claims as originally filed. In particular, support for the new claims 21-48 can be found e.g., at pages 19, lines 7-15; page 23, lines 12-29 and page 62, lines 5-14. No new matter has been added.

Cancellation or amendments of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The cancellation or amendments to the claims are being made solely to expedite prosecution of the present application. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

Sequence Compliance

The Examiner points out that Figures 1B, 5, 6, and 10 disclose sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences but are not set forth in either the Sequence Listing or the Specification by sequence identifier numbers. The Applicants amended the figure legends to recite sequence identifier numbers corresponding to these sequences.

As the Sequence Listing filed on November 2, 2001 did not contain either SEQ ID NO: 28 or 29, Applicants also submit a substitute paper and electronic copy of a replacement Sequence Listing that incorporates SEQ ID NO. 28 and 29. Because both of these sequences were disclosed in Figure 10 as of the filing date of the application, the replacement sequence listing does not contain new matter.

Rejection of Claims 1-8 under 35 U.S.C. § 112, first paragraph (written description)

Claims 1-8 have been rejected under 35 U.S.C. § 112, paragraph 1, because the specification does not describe the invention such that one skilled in the art, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner points to claims 1, 3, and 5-7 that are drawn to an isolated nucleic acid comprising a nucleotide sequence which is at least 90% identical to the nucleotide sequence set forth in SEQ ID NO: 3 or the complement thereof, which encodes a polypeptide having SEQ ID NO: 9 or having about 1-20 conservative amino acid changes of SEQ ID NO: 9. Furthermore, the Examiner avers that "to convey that the applicant was in possession of the claimed invention includes [...] determining whether the invention has been set forth in terms of distinguishing identifying characteristics as

evidenced by other descriptions of the invention...." (Office Action, page 4). Applicants respectfully traverse this rejection.

Claim 2 has been canceled, thereby rendering moot its rejection.

Applicants respectfully submit that the specification sufficiently sets forth distinguishing identifying characteristics of the claimed nucleic acid to convey that the Applicants possessed the claimed invention at the time they filed the application. For instance, the Applicants disclose both human Tid-1S and mouse Tid-1S (Examples 1 and 5, respectively). The amino acid sequence of the mouse and human proteins is very well conserved, since the two proteins differ in only 5 amino acids. Applicants further disclose a human dominant negative Tid-1S mutant, which is identical to a wild-type Tid-1S proteins except for the presence of a point mutation (H121Q; Example 3 and 7). Additionally, the Applicants describe common Tid-1S structural features that are associated with its biological activity. Indeed, Tid-1S proteins have a canonical J-domain, which Applicants have shown to be necessary for the anti-apoptotic activity of Tid-1S and has been shown to be important also in Tid-1L; a conserved splice site; a mitochondrial processing signal; and a 6 amino acid C-terminal specific sequence (SEQ ID NO: 14) (page 9, lines 18-31, page 10, lines 10-12, page 11, lines 12-13, page 21, lines 11-15 and page 59, lines 20-31). Applicants further note that the C-terminal specific sequence is identical in the human and mouse Tid-1S proteins, and further that this sequence is absent from Tid-1L proteins. In fact, Tid-1L proteins have a 33 amino acid sequence (SEQ ID NO: 13) at their C-terminus, which sequence is absent from Tid-1S proteins. Accordingly, both the J domain and the C-terminal specific sequence of Tid-1S appears to be necessary for the anti-apoptotic activity of Tid-1S proteins. Thus, contrary to the Examiner's statement, a person of skill in the art would have been able to determine which amino acids are critical to the structure or function of Tid-1S proteins based on sequence conservation at the time the application was filed.

Applicants note that, contrary to the Examiner's statement, the coding sequence of Tid-1L (SEQ ID NO: 2) does not comprise the full length SEQ ID NO: 3. Indeed, SEQ ID NO: 3 contains a C-terminal sequence (SEQ ID NO: 7) that is not included in SEQ ID NO: 2. Tid1S and Tid-1L each have different C-terminal sequences: Tid-1L has the amino acid sequence set forth in SEQ ID NO: 13 and Tid-1S has the amino acid sequence set forth in SEQ ID NO: 14.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-8 under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-8 have been rejected under 35 U.S.C. § 112, paragraph 1, because the specification does not describe the claimed invention in such a way as to enable one skilled in the are to make and/or use the invention. Specifically, the Examiner states that the "disclosure fails to describe the common attributes or characteristics that identify members of the claimed genus, and that SEQ ID NO: 3 alone is insufficient to describe the genus, because it is unpredictable whether the polypeptide variants of SEQ ID NO: 9 encoded by the claimed nucleic acid will function as hTid-1s." (Office Action, page 9). As set forth above, Applicants respectfully submit that the specification describes common attributes and characteristics that identify members of the claimed genus. Briefly, Tid-1S proteins comprise a mitochondrial cleavage site that allows the 66 N-terminal amino acids of the protein to be cleaved off. Tid-1S proteins also comprise a J domain which has been shown to be important for the anti-apoptotic activity of Tid-1S proteins and an C-terminal amino acid sequence that is specific to Tid-1S proteins and absent from Tid-1L proteins. Accordingly, based on this description, a person of skill in the art would have known at the time the application was filed where changes to the proteins can be made to obtain variants having anti-apoptotic activity or dominant negative variants of Tid-1S proteins. In addition, the specification describes assays that can be conducted for confirming the biological activity of a variant. For example, Example 3 describes assays for measuring the apoptotic or anti-apoptotic activity of a protein and Example 7 describes assays for determining the dominant negative effect of a Tid-1S variant.

Accordingly, the Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claim 2 under 35 U.S.C. § 112, second paragraph

The Examiner asserts that claim 2 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that claim 2 is vague because it recites, "the nucleotide sequence of SEQ ID NO: 2, which encodes the carboxyl-terminal 33 amino acids of SEQ ID NO: 8." Claim 2 has been canceled, thereby rendering this rejection moot.

Rejection of Claims 1 and 3-8 under 35 U.S.C. § 102(a) over Schilling et al.

Claims 1 and 3-8 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Schilling et al. (Virology 247:74-85 (1998)). Applicants respectfully traverse this rejection.

Claim 1, as amended, is drawn to an isolated nucleic acid comprising a nucleotide sequence that is at least 90% identical to the nucleotide sequence set forth in SEQ ID NO: 3 or 5 or the complement thereof and comprises SEQ ID NO: 7 or the complement thereof. Claims 3-8 depend from claim 1.

The Examiner relies on Schilling et al. as teaching "a nucleic acid (hTid-1, AF061749 of GenEmbl databes) which shares 98.6% sequences identity with SEQ ID NO: 3, and comprises 1340 bps of 1443 bps of SEQ ID NO: 3..." Applicants respectfully submit that Schilling et al. fail to disclose a nucleic acid comprising SEQ ID NO: 7. Thus, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection of Claims 1 and 3-8 under 35 USC § 102(b) over Syken et al.

Claims 1 and 3-8 have been rejected under 35 USC § 102(b) as being anticipated by Syken et al. (Proc. Natl. Acad. Sci. U.S.A. 96:8499-8504 (1999)). Applicants respectfully traverse this rejection.

Syken et al. is the Applicants' own work. A Declaration of J. Syken and K. Munger under 37 C.F.R. § 1.132 in support of this statement is attached hereto. Thus, reconsideration and withdrawal of this rejection is respectfully requested.

Conclusion

In view of the above remarks and the amendments to the claims, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Agent would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

By: _____
Lauren T. Knapp, Ph.D.
Reg. No. 45,605
Agent for Applicants

Customer ID No. 25181
Patent Group
FOLEY HOAG LLP
155 Seaport Blvd.
Boston, MA 02210
Telephone: (617) 832-1000
Facsimile: (617) 832-7000
Dated: June 16, 2003